

WHAT IS CLAIMED IS:

- 1 1. An isolated nucleic acid molecule comprising the DNA sequence set forth in Figure
2 1 (SEQ ID NO:1) or degenerate variants thereof, or fragments thereof.
- 1 2. An isolated nucleic acid molecule or degenerate variants thereof, or fragments
2 thereof, hybridizable to said DNA sequence of Claim 1 under standard
3 hybridization conditions.
- 1 3 The isolated nucleic acid molecule of either of Claims 1 or 2, which encodes a
2 polypeptide having an amino acid sequence as set forth in Figure 2 (SEQ ID
3 NO:2), or conservative variants thereof, or fragments thereof.
- 1 4. An isolated nucleic acid molecule comprising the DNA sequence set forth in SEQ
2 ID NO:3, or degenerate variants thereof or fragments thereof.
- 1 5. An isolated nucleic acid molecule or degenerate variants thereof, hybridizable to
2 said cDNA sequence of Claim 3 under standard hybridization conditions.
- 1 6. The isolated nucleic acid molecule of either of Claims 4 or 5, which encodes a
2 polypeptide having an amino acid sequence as set forth in Figure 4 (SEQ ID
3 NO:4), or conservative variants thereof or fragments thereof.
- 1 7. A detectably labeled isolated nucleic acid molecule hybridizable to an isolated
2 nucleic acid molecule as set forth in any of Claims 1, 2, 4 or 5.
- 1 8. The detectably labeled isolated nucleic acid molecule of Claim 7, wherein said
2 detectable label comprises an enzyme, a radioactive isotope, or a chemical which
3 fluoresces.
- 1 9. An isolated polypeptide comprising the amino acid sequence of Figure 2 (SEQ ID

- 1 NO:2), conservative variants thereof, fragments thereof or analogs or derivatives
2 thereof, or the amino acid sequence of Figure 4 (SEQ ID NO:4), conservative
3 variants thereof, or fragments thereof, or analogs or derivatives thereof.
- 1 10. An antibody having the polypeptide of Claim 9 as an immunogen.
- 1 11. The antibody of Claim 10, wherein said antibody is a monoclonal antibody.
- 1 12. The antibody of Claim 10, wherein said antibody is a polyclonal antibody.
- 1 13. The antibody of Claim 10, wherein said antibody is a chimeric antibody.
- 1 14. The antibody of Claim 10, wherein said antibody is detectably labeled.
- 1 15. The antibody of Claim 14, wherein a detectable label comprises an enzyme,
2 a radioactive isotope, or a chemical which fluoresces.
- 1 16. An expression vector comprising said isolated nucleic acid molecule of
2 Claim 1 operatively associated with a promoter.
- 1 17. An expression vector comprising said isolated nucleic acid molecule of
2 Claim 2 operatively associated with a promoter.
- 1 18. An expression vector comprising said isolated nucleic acid molecule of
2 Claim 4 operatively associated with a promoter.
- 1 19. The expression vector of any of Claims 16-18, wherein said promoter is
2 selected from the group consisting of the immediate early promoters of
3 hCMV, early promoters of SV40, early promoters of adenovirus, early
4 promoters of vaccinia, early promoters of polyoma, late promoters of
5 SV40, late promoters of adenovirus, late promoters of vaccinia, late

6 promoters of polyoma, the *lac* the *trp* system, the *TAC* system, the *TRC*
7 system, the major operator and promoter regions of phage lambda, control
8 regions fo fd coat protein, 3-phosphoglycerate kinase promoter, acid
9 phosphatase promoter, promoters of yeast α mating factor.

1 20. A unicellular host transformed with an expression vector of any of Claims
2 16-18.

1 21. The unicellular host according to Claim 20, wherein said host comprises *E.*
2 *coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, yeast, CHO, R1.1, B-W, L-M,
3 COS1, COS7, BSC1, BSC40, BMT10 or Sf9 cells.

1 22. A mammalian cell comprising a DNA sequence which encodes TRANCE,
2 wherein said mammalian cell is modified *in vitro* to permit higher
3 expression of TRANCE by means of a homologous recombinational event
4 consisting of inserting a promoter in functional proximity to the TRANCE
5 polypeptide encoding sequence.

1 23. A mammalian cell according to Claim 22, wherein the promoter is a
2 TRANCE polypeptide promoter and the homologous recombinational
3 event replaces a mutant TRANCE polypeptide promoter.

1 24. A method of producing an isolated polypeptide comprising the amino acid
2 sequence of Figure 2 (SEQ ID NO:2), conservative variants thereof,
3 fragments thereof or analogs or derivatives thereof, or the amino acid
4 sequence of Figure 4 (SEQ ID NO:4), conservative variants thereof, or
5 fragments thereof, or analogs or derivatives thereof, comprising the steps
6 of:

7 a) culturing a unicellular host of Claim 20 under conditions that provide for
8 expression of said isolated polypeptide; and

9 b) recovering said isolated polypeptide from said host, the culture, or both.

- 1 25. A modulator of immune response in a mammal comprising:
- 2 a) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID
- 3 NO:2), Figure 4 (SEQ ID NO:4) or conservative variants thereof, or a fragment
- 4 thereof;
- 5 b) an analog or derivative of a polypeptide having an amino acid set forth in Figure
- 6 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), or conservative variants thereof, or a
- 7 fragment thereof;
- 8 c) a fusion protein comprising an amino acid sequence of Figure 2 (SEQ ID NO:2),
- 9 Figure 4 (SEQ ID NO:4), conservative variants thereof, or a fragment thereof;
- 10 d) an antibody having an immunogen selected from the group consisting of:
- 11 i) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ
- 12 ID NO:2), Figure 4 (SEQ ID NO:4) or conservative variants thereof, or a fragment
- 13 thereof;
- 14 ii) an analog or derivative of a polypeptide having an amino acid as set
- 15 forth in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), or conservative variants
- 16 thereof, or a fragment thereof;
- 17 iii) a fusion protein wherein its amino acid sequence comprises an amino
- 18 acid sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), conservative
- 19 variants thereof, or a fragment thereof;
- 20 or
- 21 d) an anti-sense TRANCE nucleic acid comprising at least one phosphodiester
- 22 analog bond.

- 1 26. The modulator of Claim 25, wherein said modulator is an agonist of
- 2 TRANCE, and modulates immune response by increasing the life span of
- 3 mature dendritic cells and increasing T cell activation, wherein said
- 4 modulator comprises:
- 5 a) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID
- 6 NO:2), Figure 4 (SEQ ID NO:4) or conservative variants thereof, or a fragment
- 7 thereof;
- 8 b) an analog or derivative of a polypeptide having an amino acid as set forth in

9 Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), or conservative variants thereof,
10 or a fragment thereof; or

11 c) a fusion protein wherein its amino acid sequence comprises an amino acid
12 sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), conservative variants
13 thereof, or a fragment thereof.

1 27. The modulator of immune response in a mammal as set forth in Claim 25,
2 wherein said modulator is an antagonist of TRANCE and modulates
3 immune response by decreasing the life span of mature dendritic cells and
4 decreasing T cell activation, wherein said modulator comprises:

5 an antibody having an immunogen selected from the group consisting of:

6 i) a polypeptide having an amino acid sequence set forth in Figure 2
7 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4) or conservative variants thereof, or a
8 fragment thereof;

9 ii) an analog or derivative of a polypeptide having an amino acid as set
10 forth in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), or conservative
11 variants thereof, or a fragment thereof; and

12 iii) a fusion protein comprising an amino acid sequence set forth in Figure
13 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), conservative variants thereof, or a
14 fragment thereof;

15 or

16 b) an anti-sense TRANCE nucleic acid comprising at least one phosphodiester
17 analog bond.

1 28. A TRANCE agonist pharmaceutical composition comprising said
2 modulator of Claim 25 and a pharmaceutically acceptable carrier thereof.

1 29. A method for treating an immune system related condition in a mammal,
2 said method comprising the steps of:

3 a) exposing at least one mature dendritic cell of the mammal to an antigen
4 so that the at least one mature dendritic cell can present the antigen on its surface;

1 36. The method for treating an immune system related condition as set forth in
2 Claim 29, wherein said pharmaceutical composition is administered orally,
3 pulmonarily, or nasally.

1 37. A TRANCE antagonist pharmaceutical composition comprising said
2 modulator of Claim 25 and a pharmaceutically acceptable carrier thereof.

1 38. A method for treating an immune system related condition in a mammal,
2 comprising administering to the mammal a therapeutically effective amount
3 of the TRANCE antagonist pharmaceutical composition of Claim 37.

1 39. The method for treating an immune system related condition in a mammal
2 as set forth in Claim 38, wherein said condition is related to over-
3 expression of TRANCE protein in the mammal.

1 40. The method for treating an immune system related condition in a mammal
2 as set forth in Claim 39, wherein said condition is an autoimmune disease or
3 hypersensitivity to an allergen.

1 41. A method for modulating levels of expression of a TRANCE protein in a
2 mammal, comprising the steps of:
3 a) removing at least one hematopoietic stem cell from the mammal;
4 b) destroying remaining hematopoietic stem cells in the mammal;
5 c) transfecting the at least one hematopoietic stem cell with a vector comprising an
6 isolated nucleic acid molecule which encodes a TRANCE protein such that the nucleic
7 acid molecule becomes incorporated into the genome of the hematopoietic stem cell,
8 forming a transfected hematopoietic stem cell; and
9 d) introducing the transfected hematopoietic stem into the mammal so that the
10 transfected hematopoietic stem cell can self replicate and differentiate within the
11 mammal.

1 42. The method for modifying levels of expression of a TRANCE protein in a
2 mammal as set forth in Claim 41, wherein the nucleic acid molecule has a
3 DNA sequence as set forth in Figure 1 (SEQ ID NO:1) or degenerate
4 variants thereof.

1 43. A method of diagnosing an immune system related condition in a mammal,
2 wherein the method comprises the steps of:
3 a) removing a bodily sample from the mammal; and
4 b) assaying the bodily sample to determine whether TRANCE is expressed in the
5 bodily sample.

1 44. The method of diagnosing an immune system related condition in a
2 mammal as set forth in Claim 43, wherein the mammal is a human.

1 45. The method of diagnosing an immune system related condition as set forth
2 in Claim 44, wherein the TRANCE protein is encoded by a nucleic acid
3 molecule having a DNA sequence as set forth in Figure 1 (SEQ ID NO:1),
4 or degenerate variants thereof.

1 46. The method of diagnosing an immune system related condition as set forth
2 in Claim 44, wherein TRANCE has an amino acid sequence as set forth in
3 Figure 2 (SEQ ID NO:2), or conservative variants thereof.

1 47. The method of diagnosing an immune system related condition of Claim
2 43, wherein the bodily sample is blood or lymphoid tissue.

1 48. The method of diagnosing an immune system related condition of Claim 43,
2 wherein the step of assaying the bodily sample to determine whether
3 TRANCE is expressed in the bodily sample comprising contacting the
4 bodily sample to an antibody to TRANCE, and detecting the binding of the

1 antibody to TRANCE.

1 49. The method of diagnosing an immune system related condition of Claim 43,
2 wherein the step of assaying the bodily sample to determine whether
3 TRANCE is expressed in the bodily sample comprising contacting the
4 bodily sample to an isolated nucleic acid molecule hybridizable under
5 standard hybridizations to an isolated nucleic acid molecule comprising the
6 DNA sequence of SEQ ID NO:1, and detecting the hybridization of said
7 nucleic acid molecules.

1 50. The method of diagnosing an immune system related condition of Claim 43,
2 wherein said lymphoid tissue is selected from the group consisting of lymph
3 node tissue, spleen tissue, and thymus tissue.

1 51. The method of diagnosing an immune system related condition of Claim 43,
2 wherein the immune system related condition is an autoimmune disease.

1 52. A method for modulating immune response to an antigen in an animal,
2 comprising the steps of:
3 a) removing an immature dendritic cell from the animal;
4 b) pulsing the immature dendritic cell from the animal with the antigen *ex vivo*,
5 so that immature dendritic cells present the antigen on their surface;
6 b) inducing maturation of immature dendritic cells *ex vivo*;
7 c) pulsing the mature dendritic cells with a modulator of immune response *ex*
8 *vivo*;
9 d) introducing the mature dendritic cells into the animal.

1 53. The method of Claim 52, wherein the step of interacting immature dendritic
2 cells with the antigen *ex vivo* comprises:
3 a) transfecting immature dendritic cells with an expression vector comprising
4 a nucleic acid molecule which encodes the antigen, operatively associated with a

5 promoter; and

6 b) inducing expression of the nucleic acid.

1 54. The method for modulating immune response of Claim 52, wherein the
2 immature dendritic cells comprise bone marrow derived immature dendritic
3 cells.

1 54. The method of Claim 52, wherein the antigen comprises:

2 a) a pathogen, or a fragment thereof;

3 b) a virus, or a fragment thereof;

4 c) a tumor, or a fragment thereof.

1 56. A method for increasing the viability of a dendritic cell, comprising
2 contacting the dendritic cell with an isolated TRANCE comprising an
3 amino acid sequence of SEQ ID NO:2, conservative variants thereof,
4 fragments thereof, or analogs or derivatives thereof, wherein said dendritic
5 cell is contacted by said isolated TRANCE has an increased viability
6 relative to control dendritic cell not contacted with said isolated TRANCE.

1 57. The method of Claim 56, wherein the contacting of the dendritic cell with
2 said isolated TRANCE occurs *in vitro* or *in vivo*.

1 58. A method of increasing viability of a dendritic cell, comprising contacting
2 the dendritic cell with an isolated TRANCE comprising an amino acid
3 sequence of SEQ ID NO:4, conservative variants thereof, fragments
4 thereof, or analogs or derivatives thereof, wherein said dendritic cell
5 contacted by isolated TRANCE has an increased viability relative to a
6 control dendritic cell not contacted with said isolated TRANCE.

1 59. The method of Claim 58, wherein the contacting of the dendritic cell with
2 the isolated TRANCE occurs *in vitro* or *in vivo*.

- 1 60. A method of increasing viability of a dendritic cell, comprising contacting
2 the dendritic cells with an isolated TRANCE comprising an amino acid
3 sequence of SEQ ID NO:2, conservative variants thereof, fragments
4 thereof, or analogs or derivatives thereof, and contacting the dendritic cell
5 with an isolated protein which is a member of the Tumor Necrosis Factor
6 (TNF) superfamily of proteins, such that the dendritic cell comprises an
7 increased viability relative to a control dendritic cell not pulsed with
8 TRANCE and the protein.
- 1 61. The method of Claim 60, wherein the contacting steps occur
2 simultaneously.
- 1 62. The method of Claim 60, wherein the isolated protein which is a member of
2 the TNF superfamily comprises CD40L or TNF- α .
- 1 63. A method of increasing viability of a dendritic cell, comprising removing an
2 immature dendritic cell from the animal, pulsing the dendritic cell with
3 isolated TRANCE comprising an amino acid sequence of SEQ ID NO:4,
4 conservative variants thereof, fragments thereof, or analogs or derivatives
5 thereof, pulsing the dendritic cell with an isolated protein which is a
6 member of the TNF superfamily of proteins, such that the pulsed dendritic
7 cell comprises an increased viability relative to a control dendritic cell not
8 pulsed with isolated TRANCE and the isolated protein.
- 1 64. The method of Claim 63, wherein the pulsing steps occur simultaneously.
- 1 65. The method of Claim 63, wherein the isolated protein which is a member of
2 the TNF superfamily comprises CD40L and TNF- α .
- 1 66. A method for increasing viability of a dendritic cell of an animal *in vivo*,

1 comprising:

2

3 removing an immature dendritic cell from the animal;

4

5 pulsing the immature dendritic cell with an isolated TRANCE comprising an amino
6 acid sequence of SEQ ID NO:2, conservative variants thereof, fragments thereof, or
7 analogs or derivatives thereof;

8

9 inducing the immature dendritic cell to mature; and

10

11 reintroducing the mature dendritic cell into the animal.

1 67. The method of Claim 66, further comprising the step of washing the
2 dendritic cell before reintroducing the dendritic cell into the animal.

1 68. A method for increasing viability of a dendritic cell of an animal *in vivo*,
2 comprising:

3

4 Removing an immature dendritic cell from the animal;

5

6 pulsing the immature dendritic cell with an isolated TRANCE comprising an amino
7 acid sequence of SEQ ID NO:4, conservative variants thereof, fragments thereof, or
8 analogs or derivatives thereof;

9

10 inducing the immature dendritic cell to mature; and

11

12 reintroducing the mature dendritic cell into the animal.

1 69. The method of Claim 68, further comprising the step of washing the
2 dendritic cell before reintroducing the dendritic cell into the animal.

1 70. A method for increasing immune response in an animal towards an antigen,
2 comprising the steps of:

3

4 Removing removing an immature dendritic cell from the animal;

5

6 pulsing the immature dendritic cell with an isolated TRANCE comprising an amino
7 acid sequence of SEQ ID NO:2, conservative variants thereof, fragments thereof, or
8 analogs or derivatives thereof;

9

10 pulsing the immature dendritic cell with the antigen;

11

12 inducing the immature dendritic cell to mature; and

13

14 reintroducing the mature dendritic cell into the animal.

1 71. The method of Claim 70, further comprising the step of washing the
2 dendritic cell before reintroducing the dendritic cell into the animal.

1 72. The method of Claim 70, wherein the antigen comprises:

2 b) a pathogen, or a fragment thereof;

3 c) a virus, or a fragment thereof; and

4 d) a tumor, or a fragment thereof.

1 73. A method for increasing immune response in an animal towards an antigen,
2 comprising the steps of:

3

4 removing an immature dendritic cell from the animal;

5

6 pulsing the immature dendritic cell with an isolated TRANCE comprising an amino
7 acid sequence of SEQ ID NO:4, conservative variants thereof, fragments thereof, or
8 analogs or derivatives thereof;

1 pulsing the immature dendritic cell with the antigen;
2
3 inducing the immature dendritic cell to mature; and
4
5 reintroducing the immature dendritic cell into the animal.

1 74. The method of Claim 73, further comprising the step of washing the
2 dendritic cell before reintroducing the dendritic cell into the animal.

1 75. The method of Claim 73, wherein the antigen comprises:

- 2 a) a pathogen, or a fragment thereof;
3 b) a virus, or a fragment thereof; and
4 c) a tumor, or a fragment thereof.

1 76. The method of Claim 73, wherein the pulsing steps occur simultaneously.

1 77. A method for increasing immune response in an animal towards an antigen,
2 comprising the steps of:

3
4 Removing an immature dendritic cell from the animal;
5

6 pulsing the immature dendritic cell with an isolated TRANCE comprising an amino
7 acid sequence of SEQ ID NO:2, conservative variants thereof, fragments thereof, or
8 analogs or derivatives thereof;
9

10 pulsing the immature dendritic cell with an isolated protein of the TNF superfamily;
11

12 pulsing the immature dendritic cell with the antigen;
13

14 Inducing the immature dendritic cell to mature; and
15

16 reintroducing the dendritic cell into the animal.

1 78. The method of Claim 77, further comprising the step of washing the
2 dendritic cell before reintroducing the dendritic cell into the animal.

1 79. The method of Claim 77, wherein the antigen comprises:

- 2 a) a pathogen, or a fragment thereof;
- 3 b) a virus, or a fragment thereof; and
- 4 c) a tumor, or a fragment thereof.

1 80. The method of Claim 77, wherein the isolated protein of the TNF
2 superfamily comprises CD40L or TNF- α .

1 81. The method of Claim 77, wherein the steps of pulsing the dendritic cell are
2 performed simultaneously.

1 82. A method for increasing immune response in an animal towards an antigen,
2 comprising the steps of:

- 3
- 4 Removing an immature dendritic cell from the animal;
- 5
- 6 pulsing the immature dendritic cell with an isolated TRANCE comprising an amino
- 7 acid sequence of SEQ ID NO:4, conservative variants thereof, fragments thereof, or
- 8 analogs or derivatives thereof;
- 9
- 10 pulsing the immature dendritic cell with an isolated protein of the TNF superfamily;
- 11
- 12 pulsing immature the dendritic cell with the antigen;
- 13
- 14 Inducing the immature dendritic cell to mature; and
- 15

1 reintroducing the dendritic cell into the animal.

1 83. The method of Claim 82, further comprising the step of washing the
2 dendritic cell before reintroducing the dendritic cell into the animal.

1 84. The method of Claim 82, wherein the antigen comprises:

- 2 a) a pathogen, or a fragment thereof;
3 b) a virus, or a fragment thereof; and
4 c) a tumor, or a fragment thereof.

1 85. The method of Claim 82, wherein the isolated protein of the TNF
2 superfamily comprises CD40L or TNF- α .

1 86. The method of Claim 82, wherein the steps of pulsing the dendritic cell are
2 performed simultaneously.